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With reference to FIG. 2, softgel capsule, i.e. gel mass, production 200 is shown. Step 202 comprises mixing glycerin with water. The water used in step 202 may be purified by any suitable means, such as reverse osmosis, ozonation, filtration (e.g., through a carbon column) or the like. Mixing may be facilitated by an impellor, agitator, or other suitable means. Step 202 may be performed under an inert or relatively inert gas atmosphere, such as nitrogen gas N<sub>2</sub>. Heating may be performed until the temperature reaches 80° C.±5° C.

Step 204 comprises the addition of gelatin to the glycerin water mixture. Mixing may be facilitated by an impellor, agitator, or other suitable means. Step 204 may be performed under an inert or relatively inert gas atmosphere, such as nitrogen gas N<sub>2</sub>. A vacuum may be drawn in step 204 to de-aerate.

Step 206 comprises addition of a coloring agent such as a dye. A coloring agent may comprise products sold under the trademark OPATINT or other suitable agent. Step 206 may be performed under an inert or relatively inert gas atmosphere, such as nitrogen gas N<sub>2</sub>. Step 208 comprises degasing. The resulting mixture from step 208 may comprise a gel capsule material suitable for use as a gel capsule in production of a softgel capsule.

With reference to FIG. 3, softgel capsule assembly process 300 is shown. Step 302 comprises heating the fill material. The fill material may be heated to any suitable temperature. In various embodiments, the fill material is heated to 30° C.±3° C. Fill material may be heated in a fill hopper. A fill hopper may comprise a device configured to hold a volume of the fill material and/or to dispense the fill material in controlled volumes.

Step 304 comprises filling a gel mass. A gel mass may be taken from the gel capsule material produced in step 208 of FIG. 2. Filling may be performed by injecting, placing, or otherwise disposing the fill material within a volume defined by the gel capsule material. The filling may occur in an encapsulator. The spreader boxes may be a temperature of 55° C.±10° C. The wedge temperature may be 38° C.±3° C. The drum cooling temperature may be 4° C.±2° C. The encapsulator may be lubricated using MIGLYOL 812 or other suitable lubricant. Step 304 thus produces one or more softgel capsules. Filling may comprise producing a ribbon of thickness 0.85 mm±0.05 mm using spreader box knobs. The fill material may be injected into the gel to produce a fill weight having target weight ±5% (i.e., 650±33 mg and 325±16.3 mg).

Step 306 comprises drying the softgel capsules. Drying may be performed in a tumble dryer, tray dryer, or combinations thereof. For example, drying may be performed in a tumble drying basket for between about 10 minutes and about 120 minutes. Drying may continue in a drying room for about 24 hours to about 72 hours. Step 308 may comprise inspection and/or polishing. Polishing may be performed with isopropyl alcohol. Step 310 may comprise packaging. Packaging may be accomplished through any suitable means. Packaging may comprise packing softgel capsules into a blister pack, bottle, box, pouch, or other acceptable packaging.

What is claimed is:

1. A method of treating a menopause-related symptom in a woman comprising: administering to the woman an effective amount of a pharmaceutical composition, the pharmaceutical composition comprising:

solubilized estradiol;  
suspended progesterone; and  
a solubilizing agent;

wherein each of the estradiol and the suspended progesterone are present in the solubilizing agent and the estradiol and progesterone are uniformly dispersed;

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wherein at least about 90% of the estradiol is solubilized in the solubilizing agent; and

wherein the solubilizing agent comprises an effective amount at least one of mono-, di-, and triglycerides containing an ester of a C6-C12 fatty acid.

2. The method of claim 1, further comprising partially solubilized progesterone, wherein the partially solubilized progesterone is solubilized in the solubilizing agent.

3. The method of claim 1, wherein the formulation is formulated as a gelatin capsule.

4. The method of claim 1, wherein said estradiol has a dosage strength of at least about 0.125 mg and wherein said progesterone has a dosage strength of at least about 25 mg.

5. The method of claim 1, wherein the ratio of progesterone to estradiol is about 24:1, about 25:1, about 96:1, about 100:1, about 192:1, or about 200:1.

6. The method of claim 1, wherein the composition is bioequivalent to a 200 mg progesterone soft gel capsule and a 2 mg estradiol tablet.

7. A method of treating a menopause symptom in a woman comprising: administering a pharmaceutical composition to the woman, the pharmaceutical composition comprising:

solubilized estradiol;

suspended progesterone; and

a solubilizing agent, the solubilizing agent comprising an effective amount mono-, di-, and triglycerides containing an ester of a C6-C12 fatty acid;

wherein the estradiol and the suspended progesterone are present in the solubilizing agent, the estradiol and progesterone are uniformly dispersed, and at least about 90% of the estradiol is solubilized in the solubilizing agent; and

wherein the estradiol does not precipitate for at least 14 days.

8. The method of claim 7, further comprising partially solubilized progesterone, wherein the partially solubilized progesterone is solubilized in the solubilizing agent.

9. The method of claim 7, wherein the formulation is formulated as a gelatin capsule.

10. The method of claim 7, wherein said estradiol has a dosage strength of at least about 0.125 mg and wherein said progesterone has a dosage strength of at least about 25 mg.

11. The method of claim 7, wherein the ratio of progesterone to estradiol is about 24:1, about 25:1, about 96:1, about 100:1, about 192:1, or about 200:1.

12. The method of claim 7, wherein the composition is bioequivalent to a 200 mg progesterone soft gel capsule and a 2 mg estradiol tablet.

13. A method of treating a menopause symptom comprising: administering an effective amount of a pharmaceutical composition to a woman, the pharmaceutical composition comprising:

solubilized estradiol;

suspended progesterone; and

a solubilizing agent, the estradiol being stable in the solubilizing agent for at least 14 days;

wherein each of the estradiol and the suspended progesterone are present in the solubilizing agent;

wherein the estradiol and progesterone are uniformly dispersed;

wherein at least about 90% of the estradiol is solubilized in the solubilizing agent, and

wherein the solubilizing agent comprises an effective amount mono-, di-, and triglycerides containing an ester of a C6-C12 fatty acid.